

Priorities for Future IARC Monographs on the Evaluation of Carcinogenic Risks to Humans

Harri Vainio,¹ Elisabeth Heseltine,² and Julian Wilbourn¹

¹International Agency for Research on Cancer, 69372 Lyon Cedex 08, France 48201 USA;

²Communication in Science, Lajarthé, 24290 St Léon-sur-Vézère, France

The International Agency for Research on Cancer (IARC) selects chemicals, groups of chemicals, mixtures, physical and biological agents, and exposure circumstances for evaluation in its series *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans* on the basis of advice given to them by international groups of scientists. To date, 58 volumes of monographs have been published, providing evaluations of 770 agents and exposure circumstances.

The fourth group to select priorities met at IARC in Lyon 7–9 December 1993 to discuss lists of agents and exposures that had been proposed by some 150 scientists at major national cancer research centers and at other national and international institutions and to recommend whether they should be given high or low priority for consideration or reconsideration within monographs planned for 1995–2000 or whether they should be deleted from the lists. The suggestions were classified loosely as occupational exposures/industries, physical factors, industrial chemicals, fibers, medical treatments, pesticides, food additives and contaminants, naturally occurring substances, environmental contaminants, and biological agents. The lists were supplemented by priority data sheets that had been completed for each agent or exposure by the person nominating it for consideration. The sheets contained the CAS number and formula of the agent

(if applicable), whether the evaluation would be a new one or a re-evaluation, and a brief justification for the nomination. In all 267 nominations were considered. The high and low priorities accorded by the working group to various agents and exposure circumstances are shown in Table 1.

The group proposed grouping certain agents to reflect particular chemical classes, such as aldehydes, nitrotoluenes, chlorophenoxy herbicides, dithiocarbamates and the class of fungicides that includes folpet, captan, and phosmet; sucrose, lactose, and other disaccharides; artificial sweeteners; and antioxidants. The group also recommended that IARC organize meetings or workshops to attempt to summarize current knowledge on the relevance of generic mechanism of action to carcinogenic risk to humans, before evaluating evidence for the carcinogenicity of individual agents that may act by the mechanism in question. Examples of such mechanisms are peroxisome proliferation, particle carcinogenesis, and thyrostatic effects.

The group also recommended that IARC organize meetings or workshops on the effects on cancer occurrence of diet and of sexual and reproductive behavior. Although certain components of diet might be amenable to consideration within the structure of the monographs, it was considered that elements such as fat and caloric intake were not. These issues could be addressed by the agency's

Scientific Publications series.

The working groups that evaluate agents and exposures for carcinogenicity refer for biological and epidemiological data only to primary reports that have been published in the openly available scientific literature or to primary information that is in the public domain, such as government reports that have undergone peer review and are widely available. The purpose of this restriction is to make it possible for readers of the monographs to verify the information and conclusions, thus ensuring the transparency of the evaluations in the monographs.

Many of the priorities listed above can be incorporated into plans for monographs in 1995–2000; for some of those given low priority, however, inclusion depends to a large extent on the availability of published data. A plea is therefore made that anyone involved in studies that are planned, in progress, or already completed ensure that the results are published in the scientific literature as rapidly as possible. A large body of both positive and negative information exists on several of the agents listed that have been accorded high priority for evaluation. It is hoped that any additional data will be made available in a suitably published form in time for meetings at which the agents and exposures are scheduled for evaluation. The full report of the meeting was published as IARC Internal Report no. 93/005 and is available upon request.

Address correspondence to H. Vainio, Unit of Carcinogen Identification and Evaluation, International Agency for Research on Cancer, 150 cours Albert-Thomas, 69372 Cedex 08, France.

The full report of the meeting was published as IARC Internal Report no. 93/005 and is available upon request.

PARTICIPANTS IN THE AD-HOC WORKING GROUP TO PROPOSE PRIORITIES FOR THE IARC MONOGRAPHS

Chair

B. Terracini, Unit of Cancer Epidemiology, Department of Biomedical Science and Human Oncology, Turin, Italy

Vice-Chair

B.W. Stewart, Children's Leukaemia and Cancer Research Centre, The Prince of Wales Children's Hospital, Randwick, Sydney, Australia

Rapporteur

L. Fishbein, Princeton Scientific Publishing Co., Washington Office, Annandale, Virginia

Working Group

M. De Smedt, Commission of the European Communities, Luxembourg

E. Dybing, National Institute of Public Health, Oslo

H. Galal Gorchev, International Programme on Chemical Safety, World Health Organization, Geneva

R.A. Griesemer, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina

J.M. Harrington, University of Birmingham, Birmingham, UK

B. Holmberg, National Institute of Occupational Health, Solna, Sweden

R.O. McClellan, Chemical Industry Institute of Toxicology, Research Triangle Park, North Carolina

S. Olin, International Life Sciences Institute, Risk Science Institute, Washington, DC

E.K. Silbergeld, University of Maryland Medical School, Baltimore, Maryland

M. Takahashi, National Institute of Health Sciences, Tokyo

H. Tulinius, Icelandic Cancer Registry, Reykjavik, Iceland

M.D. Waters, Health Effects Research Laboratory, U.S. Environmental Protection Agency, Research Triangle Park, North Carolina

Table 1. Agents and exposures accorded high and low priority for consideration within the *IARC Monographs* series

Agent or exposure	Priority	Agent or exposure	Priority	Agent or exposure	Priority
Occupational exposures/industries					
Agricultural workers	High	Ethyl benzene	Low	Paraquat and diquat	Low
Aluminum production ^a	High	Ethylene glycol	Low	Phosmet	Low
Dry cleaners using tri- and/or tetrachloroethylene ^a	High	Gallium compounds	Low	Propazine	Low
Electrical workers	High	Gasoline ^a	Low	Propiconazole	Low
Leather goods manufacture ^a	High	Glutaraldehyde	Low	Tecnazene	Low
Pulp and paper manufacture ^a	High	Glycidyl trimethylammonium chloride	Low	Triadimefon	Low
Printing and printing inks	High	Hexachloroethane ^a	Low	Vinclozin	Low
Rubber industry ^a	High	Hydrogen peroxide ^a	Low	Food additives and contaminants	
Butchers and meat workers	Low	Indium phosphate	Low	Aspartame	High
Chemists and other laboratory workers	Low	2-Mercaptobenzothiazole	Low	Butylated hydroxytoluene ^a	High
Chimney sweeps	Low	Methyl carbamate ^a	Low	Saccharin ^a	High
Cooks, professional	Low	4-Methylquinoline	Low	Sugar substitutes such as lactitol	High
Electronics industry	Low	1-Naphthylamine ^a	Low	trans-Anethole	
Petroleum refining ^a	Low	Perfluorooctanoic acid and ammonium perfluorooctanoate	Low	Fast Green FCF ^a	Low
Physical factors		<i>o</i> -, <i>m</i> -, <i>p</i> -Phenylenediamines ^a	Low	Musk xylol	Low
Electric and magnetic fields	High	Quinoline	Low	Propyl gallate	Low
Industrial chemicals		Rhodamine 6G ^a	Low	Naturally occurring substances	
Acrolein ^a	High	Titanium dioxide ^a	Low	Betel quid (without tobacco) ^a	High
Bitumens ^a	High	Titanocene dichloride	Low	Caffeine and caffeine-containing beverages ^a	High
Carbon blacks ^a	High	2,4- and 2,6-Toluene diisocyanates ^a	Low	Fusarium toxins ^a	High
3-Chloro-2-methylpropene	High	<i>m</i> -Toluidine	Low	Naphthalene	High
4-Chloro- <i>o</i> -toluidine	High	<i>p</i> -Toluidine	Low	Nitrates	High
5-Chloro- <i>o</i> -toluidine	High	1,3,5-Triglycidyl isocyanurate	Low	Nitrites	High
Crotonaldehyde	High	Fibers		3-Nitroso(methylamino)propionaldehyde ^a	High
2,3-Dibromo-1-propanol	High	Asbestos ^a	High	3-Nitroso(methylamino)propionitrile ^a	High
1,3-Dichloro-2-propanol	High	Man-made mineral fibers ^a	High	4-Nitroso(methylamino)-1-(3-pyridyl)-1-butanol ^a	High
2,4- and 2,6-Dinitrotoluenes	High	Silica ^a	High	4-Nitroso(methylamino)-1-(3-pyridyl)-1-butanone ^a	High
1,2-Diphenylhydrazine	High	Medical treatments		<i>N</i> '-Nitrosomornicotine ^a	High
2,3-Epoxy-1-propanol	High	Anthraquinones (1-Hydroxyanthraquinone)	High	Ozone	High
Formaldehyde ^a	High	Benzodiazepines ^a	High	Phomopsis A	High
Glycol ethers	High	Benzoyl peroxide ^a	High	Protein thermolysis products	High
Lead, inorganic ^a	High	Chloral hydrate	High	Quercitina	High
Methyl- <i>tert</i> -butyl ether	High	5-Fluorouracil ^a	High	Sucrose and its thermolysis products	High
Monochlorobenzene	High	Iodine-131	High	Agaritine ^a	Low
Nitrobenzene	High	Nucleoside analogs (AZT, DDI)	High	Benzyl acetate ^a	Low
N-Nitrosodiethanolamine ^a	High	Oral contraceptives (estrogens) ^a	High	Capasaicin	Low
Nitrotoluenes	High	Tamoxifen	High	Cholesterol, dietary ^a	Low
Polybrominated flame retardants and contaminants	High	Triamterene	High	Ethanol ^a	Low
Polychlorinated dibenzo- <i>p</i> -dioxins and dibenzofurans ^a	High	Vitamin K (by injection in neonates)	High	Malonaldehyde	Low
Tetrahydrofuran	High	Amphetamines	Low	Myristicin	Low
Tetranitromethane	High	Antidepressants (amitryptiline, fluoxetine)	Low	Pyrolizidine alkaloids	Low
<i>o</i> -Toluidine ^a	High	Carbadox	Low	Tannins and tannic acid ^a	Low
1,1,1-Trichloroethane	High	Coumarin	Low	Environmental contaminants	
Trichloroethylene ^a	High	Doxylamine succinate	Low	Air pollution	High
2,4,6-Trinitrotoluene	High	Gentian violet	Low	Benzo[<i>a</i>]pyrene ^a	High
Tris(2-chloroethyl)phosphate ^a	High	6-Mercaptopurine ^a	Low	Environmental tobacco smoke	High
Vinyl fluoride ^a	High	8-Methoxypsoralen ^a	Low	Halogenated by-products in water	High
Acetamide ^a	Low	Omeprazole	Low	Wastes, solid and hazardous	High
Acrylic acid ^a	Low	Phenobarbital ^a	Low	Biological agents	
3-Amino-9-ethylcarbazole hydrochloride	Low	Tolbutamide	Low	Carbazole ^a	Low
4-Amino-3-fluorophenol	Low	Urocanic acid	Low	Chrysene ^a	Low
Aniline ^a	Low	Pesticides		3,7-Dinitrofluoranthene ^a	Low
Bis(2-chloroethyl)ether ^a	Low	Alachlor	High	3,9-Dinitrofluoranthene ^a	Low
Boric acid	Low	Benomyl	High	Fly ash	Low
<i>tert</i> -Butyl hydroquinone	Low	3-Chloro-2-methylpropene	High	9-Methylcarbazole	Low
Carbon disulfide	Low	<i>p</i> -, <i>p</i> -DDT ^a	High	1-Methylnaphthalene	Low
Chlorofluorocarbons	Low	2,4-D and other chlorophenoxy compounds ^a	High	4-Methylquinoline	Low
<i>N</i> -Chloroformyl morpholine	Low	Ethylene and propylene bis(dithiocarbamates)	High	Pyrene ^a	Low
1-Chloro-2-nitrobenzene	Low	Folpet	High	Biological agents	
1-Chloro-4-nitrobenzene	Low	Hexachlorobenzene ^a	High	Epstein-Barr virus	High
Chrysoidine ^a	Low	Captan ^a	Low	Human immunodeficiency virus	High
CI Direct Blue 218	Low	Chinomethionat	Low	Human papilloma virus	High
Cutting fluids, synthetic	Low	Crotoxyphos	Low	Human T-cell leukemia virus type 1	High
3,3'-Diaminobenzene	Low	Glyphosate	Low	Herpes simplex virus	High
Dimethyl methyl phosphonate	Low	Isoproturon	Low		
Dinitrobenzenes	Low	Linuron	Low		
Ethanol ^a	Low	Malathion	Low		
		Monuron TCA	Low		

^aReevaluation.